

REPLY

Serial No. 10/020,596  
Atty. Docket No. GP123-02.UTAmendments to the Claims

1. (Currently Amended) A method for ~~forming a duplex from a polynucleotide probe and determining the presence of~~ a target nucleic acid in a sample, said method comprising: providing the following to a test sample:

a) providing to a sample a negatively charged polynucleotide probe and a synthetic, water soluble polycationic polymer, wherein said probe is provided to said sample under conditions permitting said probe to preferentially hybridize to a target nucleic acid, if present, which may be present in said sample, thereby forming a probe:target duplex, and wherein said a synthetic polyeationie polymer is provided to said sample in an amount sufficient to increase the association rate of said probe and said target nucleic acid in said sample under said conditions; and

b) exposing said sample to a dissociating reagent in an amount sufficient to dissociate said polymer from said probe and said target nucleic acid duplex after said probe and said target nucleic acid have had sufficient time to associate in said sample; and

c) determining whether said duplex is present in said sample as an indication of the presence or absence of said target nucleic acid.

2. (Original) The method of claim 1, wherein the cationic monomers comprising said polymer are in molar excess of the phosphate groups of said probe.

3. (Original) The method of claim 1, wherein said polymer is a copolymer.

4. (Original) The method of claim 1, wherein said polymer is a graft copolymer.

5. (Original) The method claim 1, wherein said polymer has a delocalized charge.

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6. (Original) The method of claim 1, wherein the concentration of said polymer in said sample is in the range of about 10  $\mu$ M to about 100  $\mu$ M.

7. (Original) The method of claim 1, wherein said polymer has a weight average molecular weight of less than about 300,000 Da.

8. (Original) The method of claim 1, wherein said probe includes multiple interacting labels and comprises first and second base regions which hybridize to each other under said conditions in the absence of said target nucleic acid, wherein said labels interact with each other to produce a first detectable signal when said probe is not hybridized to said target nucleic acid and a second detectable signal when said probe is hybridized to said target nucleic acid, and wherein said first and second signals are detectably different from each other.

9. (Original) The method of claim 8, wherein said probe includes a third base region which hybridizes to said target nucleic acid under said conditions, and wherein said third base region is distinct from said first and second base regions or said third base region partially or fully overlaps at least one of said first and second base regions of said probe.

10. (Original) The method of claim 1, wherein said probe is a polyanion.

11. (Original) The method of claim 10, wherein said probe further includes at least one of a cationic group and a nonionic group.

12. (Original) The method of claim 10, wherein the distance between adjacent cationic monomers of said polymer approximates the distance between adjacent phosphate groups of said probe and said target nucleic acid.

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13. (Original) The method of claim 1, wherein said target nucleic acid comprises RNA.

14. (Original) The method of claim 13, wherein said RNA is ribosomal RNA.

15. (Original) The method of claim 13, wherein said RNA is messenger RNA.

16. (Original) The method of claim 1, wherein a complex comprising said polymer is formed in said sample under said conditions.

17. (Original) The method of claim 16, wherein said complex includes a plurality of polymers which are covalently linked.

18. (Original) The method of claim 16 wherein said complex includes polymers and polynucleotides which are covalently linked.

19. (Original) The method of claim 16, wherein said complex is water soluble.

20. (Original) The method of claim 1, wherein said probe and said polymer are in solution during the formation of said duplex.

21. (Original) The method of claim 1, wherein the association rate of said probe and said target nucleic acid under said conditions and in the presence of said polymer is at least about 2-fold greater than the association rate of said probe and said target nucleic acid under said conditions and in the absence of said polymer.

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22. (Original) The method of claim 1, wherein the association rate of said probe and said target nucleic acid under said conditions and in the presence of said polymer is at least about 5-fold greater than the association rate of said probe and said target nucleic acid under said conditions and in the absence of said polymer.

23. (Original) The method of claim 1, wherein the association rate of said probe and said target nucleic acid under said conditions and in the presence of said polymer is at least about 10-fold greater than the association rate of said probe and said target nucleic acid under said conditions and in the absence of said polymer.

24. (Original) The method of claim 1, wherein the association rate of said probe and said target nucleic acid under said conditions and in the presence of said polymer is at least about 100-fold greater than the association rate of said probe and said target nucleic acid under said conditions and in the absence of said polymer.

25. (Original) The method of claim 1, wherein the association rate of said probe and said target nucleic acid under said conditions and in the presence of said polymer is at least about 1000-fold greater than the association rate of said probe and said target nucleic acid under said conditions and in the absence of said polymer.

26. (Canceled)

27. (Previously Amended) The method of claim 1, wherein said dissociating reagent is at least one of a polyanion or an anionic detergent.

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28. (Original) The method of claim 1, wherein said conditions include a temperature of at least about 40°C and a salt concentration of at least about 5 mM monovalent cations or an equivalent salt concentration containing multivalent cations.

29. (Original) The method of claim 28, wherein said temperature is up to about 60°C.

30. (Original) The method of claim 1, wherein said conditions include a temperature of at least about 40°C and a salt concentration of at least about 150 mM monovalent cations or an equivalent salt concentration containing multivalent cations.

31. (Original) The method of claim 30, wherein said temperature is up to about 60°C.

32. (Original) The method of claim 1, wherein said polymer is provided to said sample before said probe.

33. (Canceled)

34. (Currently Amended) The method of claim ~~33~~ 1, wherein ~~said probe preferentially hybridizes to a target nucleic acid sequence contained in said target nucleic acid under said conditions and~~ said determining step is diagnostic for the presence or absence of a virus or organism or members of a group of viruses or organisms in said sample.

35. (Original) The method of claim 34, wherein said probe stably hybridizes to one or more nucleic acid sequences present in said sample having at least a single base difference from said target nucleic acid sequence.

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36. (Original) The method of claim 33, wherein said probe includes a label.

Claims 37-60 (Canceled)

61. (New) The method of claim 1, wherein said probe and said polymer are independently provided to said sample.